

Application No.: 08/444,790

Docket No.: 01017/40451B

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the applications:

Listing of Claims:

Claims 1-61 (canceled)

62. (currently amended) A protein comprising

(a) a soluble fragment of a receptor, ~~that wherein the receptor~~ (i) specifically binds human tumor necrosis factor (TNF), (ii) has an apparent molecular weight of ~~about 55 kilodaltons or~~ about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, and (iii) comprises a fragment of the amino acid sequence set forth in SEQ ID NO: [[2 or]] 4; and  
(b) all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region;

wherein said protein specifically binds human TNF.

Claims 63-65 (canceled)

66. (currently amended) A purified protein comprising

(a) a soluble fragment of a receptor, ~~that wherein the receptor~~ (i) specifically binds human tumor necrosis factor, (ii) has an apparent molecular weight of ~~about 55 kilodaltons or~~ about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, and (iii) is encoded by a nucleic acid sequence comprising a fragment of the DNA sequence set forth in SEQ ID NO: [[1 or ]] 3; and

(b) all of the domains of the constant region of a human immunoglobulin heavy chain other than the first domain of said constant region;

wherein said protein specifically binds human TNF.

67. (previously presented) The protein of claim 66, wherein the protein is recombinantly produced.

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Claims 68-101 (canceled)

102. (currently amended) The protein of claim 62 or 66 [[101]] wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8).

103. (previously presented) The protein of claim 102 wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

104. (currently amended) The protein of any one of claims 62 or ~~100-103~~ 66, wherein said human immunoglobulin heavy chain is an IgG heavy chain.

105. (currently amended) The protein of claim 104 wherein the IgG-said human immunoglobulin heavy chain is IgG<sub>1</sub> or IgG<sub>3</sub>.

106. (currently amended) A protein comprising  
(a) a soluble fragment of a receptor, that wherein the receptor (i) specifically binds human tumor necrosis factor (TNF), (ii) has an apparent molecular weight of ~~about 55 kilodaltons or about 75 kilodaltons~~ on a non-reducing SDS-polyacrylamide gel, and (iii) comprises a fragment of the amino acid sequence set forth in SEQ ID NO: 4, wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8) and LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10); and  
(b) all of the domains of the constant region of a human IgG<sub>1</sub> heavy chain other than the first domain of said the constant region;  
wherein said protein specifically binds human TNF.

107. (currently amended) A recombinant protein encoded by a polynucleotide which comprises two nucleic acid subsequences,

(a) one of said subsequences encoding a soluble fragment of an insoluble human TNF receptor protein having an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel, said soluble fragment comprising a fragment of the amino acid sequence of SEQ ID NO: [[2 or]] 4, and

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(b) the other of said subsequences encoding all of the domains of the constant region of the heavy chain of a human immunoglobulin other than the first domain of said constant region,

wherein said recombinant protein specifically binds human TNF.

Claims 108 and 109 (canceled)

110. (currently amended) The protein of claim 109-107, wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO: 12) and VFCT (SEQ ID NO: 8).

111. (previously presented) The protein of claim 110 wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

112. (currently amended) The protein of any one of claims [[107-111]] 107, 110 or 111 wherein said human immunoglobulin heavy chain is an IgG heavy chain.

113. (currently amended) The protein of claim 112 wherein the IgG said human immunoglobulin heavy chain is IgG<sub>1</sub> or IgG<sub>3</sub>.

114. (currently amended) A pharmaceutical composition comprising the recombinant protein of any of claims 62, 66, 107, 134 or [[100-113]] 135 and a pharmaceutically acceptable carrier material.

Claims 115-118. (canceled)

119. (new) The protein of claim 62, wherein the protein is purified.

120. (new) The protein of claim 62, wherein the protein is produced by CHO cells.

121. (new) The protein of claim 62, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human immunoglobulin heavy chain other than the first domain of the constant region.

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122. (new) The protein of claim 66, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human immunoglobulin heavy chain other than the first domain of the constant region.

123. (new) The protein of claim 104 wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4H $\gamma$ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314) or by pCD4-H $\gamma$ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5523).

124. (new) The protein of claim 105 wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4H $\gamma$ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314).

125. (new) The protein of claim 106, wherein the protein is purified.

126. (new) The protein of claim 106, wherein the protein is produced by CHO cells.

127. (new) The protein of claim 106, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human IgG<sub>1</sub> heavy chain other than the first domain of the constant region.

128. (new) The protein of claim 106, wherein the soluble fragment comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

129. (new) The recombinant protein of claim 107, wherein the recombinant protein is purified.

130. (new) The recombinant protein of claim 107, wherein the recombinant protein is produced by CHO cells.

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131. (new) The recombinant protein of claim 107, wherein the protein consists of (a) the soluble fragment of the receptor and (b) all of the domains of the constant region of the human IgG<sub>1</sub> heavy chain other than the first domain of the constant region.

132. (new) The protein of claim 112 wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by pCD4Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314) or by pCD4-Hy3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5523).

133. (new) The protein of claim 113 wherein said domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin amino acid sequence encoded by the DNA insert of pCD4Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314).

134. (new) A protein consisting of  
(a) a soluble fragment of an insoluble human TNF receptor, wherein the receptor (i) specifically binds human TNF, and (ii) has an apparent molecular weight of about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel,  
wherein the soluble fragment comprises the peptides LCAP (SEQ ID NO:12) and VFCT (SEQ ID NO:8), and  
(b) all of the domains of the constant region of a human IgG<sub>1</sub> heavy chain other than the first domain of the constant region,  
wherein the protein specifically binds human TNF, and  
wherein the protein is produced by CHO cells.

135. (new) The protein of claim 134, wherein the soluble fragment comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10).

136. (new) The protein of claim 134, wherein the protein is purified.

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137. (new) A pharmaceutical composition comprising the recombinant protein of claim 105 and a pharmaceutically acceptable carrier material.